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ORIGINAL PAPER

Population-specific serum creatinine centiles in neonates with posterior urethral valves already predict long-term renal outcome

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Abstract

Introduction: The lowest serum creatinine (nadir Scr, cut-off 1 mg/dl) during infancy predicts subsequent renal outcome in posterior urethral valve (PUV) infants, but early, neonatal values may be useful to guide care. We aimed to explore correlations between neonatal Scr values and long-term renal outcome.

Methods: Retrospective evaluation of records of 39 PUV patients, treated in the University Hospitals Leuven (2001–2011). Scr measurements were collected and associations (Mann–Whitney U, Spearman) to predict unfavorable renal outcome [GFR <60 ml/min/1.73 m^2 at 2 years] were explored.

Results: Unfavorable renal outcome at the last follow-up was observed in 7/36 patients (19%). Besides the nadir Scr at a median age of 5 months, also the peak Scr and Scr between days 9 and 42 correlated significantly with renal outcome. By introducing "centiles" for neonatal Scr values in this PUV cohort, the 75th Scr percentile in this PUV cohort was highly predictive for unfavorable renal outcome.

Conclusions: Besides the nadir Scr, early neonatal Scr values (peak, days 9–42, PUV cohort-specific 75th centile) also predicted unfavorable renal outcome. The introduction of PUV disease specific reference Scr centiles may be helpful to facilitate earlier prediction and guide counseling, but necessitates external validation.

Keywords

Congenital malformations, creatinine, posterior urethral valves, prognosis, renal failure

History

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Introduction

Posterior urethral valves (PUV) are the most common cause of congenital urethral tract obstruction (1 in 5000–8000 children) and responsible for relevant long-term nephro-urological morbidities such as vesico-ureteral reflux (VUR), bladder dysfunction, and chronic kidney disease (CKD). About 15–20% of the patients will indeed evolve to end stage renal disease (ESRD) [1–3]. To further improve renal outcome, neonatal identification of patients at risk for CKD is important.

Several authors described an association between serum creatinine (Scr) values during infancy and renal outcome [2,4–9]. In fact, most authors agree that the 'nadir' Scr (i.e. the lowest value, threshold 1 mg/dl) in infancy accurately predicts long-term renal prognosis [1,2,4–6,9]. However, determination of the nadir Scr requires meticulous follow-up, and it is not yet available in early infancy. Denes et al. [4] demonstrated that Scr levels 4–5 d after the initial diagnosis correlate strongly with long-term renal outcome. Sarhan et al. [1,9] described that initial Scr, nadir Scr, creatinine clearance (CL_{cr}) at the age of 1 year, and renal parenchymal echogenicity on initial renal ultrasound correlated significantly with long-term renal outcome. Reports about the prognostic value of Scr trends in neonates in PUV cases are limited. Deshpande et al. [5] introduced such a ''prediction trend curve''. These authors also confirmed that the peak Scr was at about day 5 of postnatal life with subsequent decrease until 2 months. This pattern is similar to the initial raise and subsequent decrease in Scr in other reference neonatal populations and data throughout infancy [1,10–12].

Our study intends to describe Scr trends in a cohort of PUV neonates and compare these findings with reference Scr values in neonates admitted in the same unit for PUV-unrelated causes. We subsequently aimed to investigate whether these trends had any predictive value for the long-term renal outcome in PUV patients.

Methods

Study population and data collection

The Ethics Board of the University Hospitals Leuven, Belgium, approved the study protocol and its reporting (ML 9708). To enlist all patients with PUV treated in the

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of Scr values (peak Scr, but also 3–6th week) within this PUV population were significant predictors of subsequent unfavorable renal outcome.

The overall nephro-urological outcome is similar to other cohorts reported [1–9,18]. CKD Stage ≥3 was documented in 11% and 19% at 2 years and at latest follow-up, respectively, while persistent diurnal incontinence at 5 years (33%), ureter reimplantation (46%) and treatment for arterial hypertension (25%) were common (Table 3). Although we are aware that all above-mentioned aspects contribute to the overall morbidity and that adequate management of these aspects itself also affects subsequent renal outcome, our focus was to link Scr values of PUV cases with subsequent renal outcome. We hereby explored the nadir Scr in the first year of life, the use of reference Scr centile values in neonates and finally, the use of PUV population-specific Scr centiles as predictors of renal outcome.

The nadir Scr in the first year of life has already been described as a valid predictor of long-term renal outcome [1,2,4–6,9]. We confirmed this correlation between nadir Scr and estimated ($r = -0.67$; 95% CI −0.85 to −0.34; $p = 0.0007$) or measured GFR ($r = -0.54$, 95% CI − 0.82 to −0.06; $p = 0.03$) at 2 years [4,6,7,9,10,18] with a cut-off value of 1 mg/dl for renal impairment (≥CKD3) in this cohort. However, this nadir Scr [0.49, range 0.17–2.21 mg/dl] was only attained at a median age of 5 (range 1.5–12) months. Our aim was to explore to what extent Scr in neonatal life or early infancy (birth–day 42) already reflects unfavorable renal outcome.

Obviously, such an exercise is hampered by the physiological Scr fluctuations in early infancy. Postnatal life is characterized by an initial Scr increase, most pronounced in the most immature neonates, with a subsequent decrease, most delayed in the most immature neonates [10,15]. Since this pattern was also observed in the current PUV cohort, we first aimed to compare the individual Scr values in PUV cases with centile reference values recently reported from the same neonatal unit [10,15]. Unfortunately, since almost all neonatal Scr values in our PUV population were in the upper quartile (peak Scr value >P75 in 89% PUV patients, and peak Scr value >P90 in 85% PUV patients), this approach could not discriminate between '*high*' and '*too high*' Scr values to predict unfavorable renal outcome.

However, we documented significant correlations between the neonatal Scr values and long-term renal outcome: peak Scr, Scr values from day 9 of life onwards up to day 42 correlated significantly with GFR at age 2 years. Consequently, a centile curve with population-specific ''reference'' Scr values for PUV patients (Table 2) was established. Using this approach, a significant link between Scr values either above or below this 75th centile P75 or <P75 and the long-term renal outcome was documented. PUV patients with neonatal Scr values in the upper quartile of this PUV percentile curve (e.g. peak Scr >P75) had a significantly worse renal outcome (median estimated GFR 25.75 versus 76.6 ml/min/1.73 m^2, $p = 0.014$) at 2 years. This was documented for Scr measurements starting days 9–42 of life, and for the peak Scr (Figure 3).

We are very much aware that the number of PUV cases was too limited to make any firm conclusions.

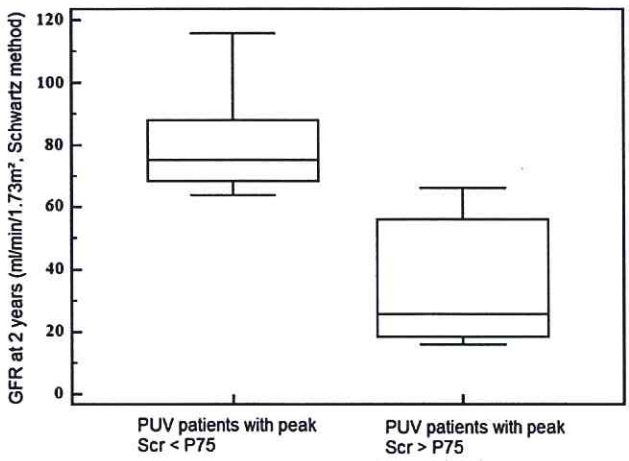

Figure 3. Relation between neonatal peak Scr values in patients with PUV and the estimated GFR using a dichotomous approach > or < P75 calculated in the PUV population calculated with the Mann–Whitney U test. The first group (peak Scr < P75) has a significantly better estimated GFR (median 75.17 ml/min/1.73 m^2 > CKD Stage 3; range 63.97–115.64 ml/min/1.73 m^2) than the second group (peak Scr > P75) (median 25.75 ml/min/1.73 m^2 < CKD Stage 3; range 16.15–66.17 ml/min/1.73 m^2).

However, given our findings, prospective validation on the use of PUV-specific centiles in different centers might be a useful next step. Another weakness of this study relates to the use of Scr itself to estimate renal function [19]. We are aware that other biomarkers like cystatin C in blood, or transforming growth factor-β1 (TGF-β1), tumor necrosis factor-α (TNF-α), interleukin-6 (IL-6), and microalbumin in urine may be promising to predict the subsequent renal outcome [3,20]. Similarly, fetal urine and ultrasound-related biomarkers have been suggested to improve prediction of postnatal renal outcome and can be used when fetal surgery is considered [21,22]. This, however, at least necessitates a fetal bladder puncture and a prenatal diagnosis [21,22].

Consequently, Scr is at present still the most readily accessible, available method to estimate renal function and generally used throughout literature to perform CKD risk stratification [1,2,3,8–11,18]. Related to the estimated renal function based on Scr observations, we both estimated and measured GFR repeatedly during the first year of life and throughout childhood. For the estimates, we used the Schwartz formula, a generally accepted and often applied estimate of GFR [16]. From the age of 1 to 1.5 year onwards, we also had access to individual measured (Cr EDTA or inulin clearance).

Taking the above-mentioned limitations into account, this study provides contemporary data (2001–2011) on the overall nephro-urological outcome in a cohort of 39 PUV cases and suggests using PUV cohort-specific Scr centiles to predict renal outcome. We hereby provide evidence that – in addition to the nadir Scr – early neonatal Scr values (peak, days 9–42 or 75th centile for this specific population) indeed already predict unfavorable renal outcome. PUV-specific reference Scr centiles may facilitate earlier prediction and counseling, but this claim necessitates prospective external validation.

peak Scr to Scr at age 3 months in our study is 90% of the total decrease from peak to nadir Scr. At the age of 3 months, we found a median decrease of 60% in Scr from the peak value.

Compared with reference Scr observations [1,8,26], PUV neonates had significantly higher Scr values: 88.9% of them had a peak Scr value >P75, and 85.2% of them even >P90. At 6 weeks of age, 2/3 and 1/3 PUV cases, respectively, had Scr values above the 75th and 90th centile of reference Scr values. In essence, because almost all Scr in PUV cases were above the 75th or even 90th centile, these reference Scr thresholds were not significant predictors of subsequent unfavorable renal outcome. In contrast, the 75th centile peak Scr value (2.23 mg/dl, Table 2), but also Scr observations between the 3rd and 6th week within the PUV cohort were significant predictors of subsequent unfavorable renal outcome (e.g. correlation peak Scr < p75 and estimated GFR at 2 years, Figure 3).

Discussion

The overall nephro-urological outcome and risk factors for unfavorable renal outcome (GFR <60 ml/min/1.73 m^2) were described in a cohort of 39 PUV cases. About 20% of PUV cases had unfavorable renal outcome, unrelated to pre- or postnatal diagnosis. Median Scr values in early infancy in PUV cases were higher when compared with reference Scr observations [10,15]. Scr observations above the 75th centile

Table 2. Scr values (mg/dl) in early infancy in PUV patients ($n = 39$).

Day	P50	P25–P75	P90	Range
0 ($n = 18$)	0.72	0.62–0.81	0.86	0.44–0.90
1 ($n = 15$)	1.27	1.15–1.47	1.61	0.80–1.93
2 ($n = 16$)	1.39	1.27–1.70	2.04	0.68–2.20
3 ($n = 17$)	1.30	1.17–1.81	2.05	0.85–2.75
4 ($n = 18$)	1.24	1.08–1.66	2.05	0.58–2.62
5 ($n = 18$)	1.09	0.96–1.60	2.43	0.72–2.73
6 ($n = 17$)	1.18	0.98–1.52	1.96	0.57–2.65
7 ($n = 18$)	0.99	0.83–1.38	2.04	0.55–2.86
8 ($n = 15$)	0.91	0.78–1.33	2.28	0.58–3.06
9 ($n = 12$)	1.04	0.79–1.85	4.13	0.67–6.50
14 ($n = 22$)	0.88	0.70–1.20	3.25	0.39–5.47
21 ($n = 21$)	0.82	0.71–1.55	2.4	0.52–3.78
28 ($n = 20$)	0.81	0.64–1.30	2.43	0.48–3.86
42 ($n = 21$)	0.62	0.52–0.86	1.74	0.22–2.59
Peak Scr ($n = 27$)	1.60	1.34–2.23	2.92	0.67–6.50
Nadir Scr ($n = 29$)	0.56	0.28–0.84	1.01	0.17–2.21

The number of Scr observations, percentiles (P50, P25–75, and P90), and range of Scr values are provided.

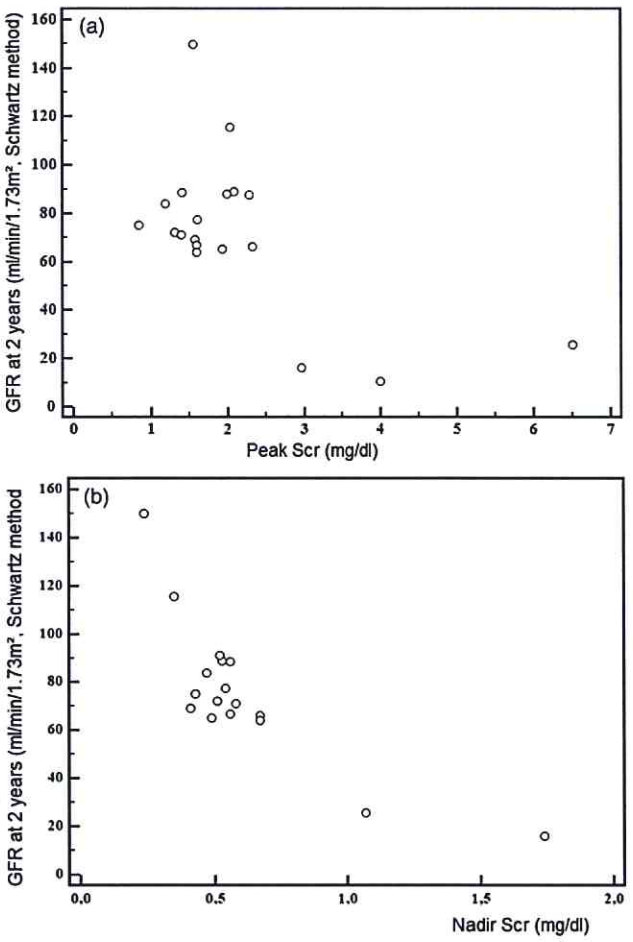

Figure 2. (a) There is a significant correlation between the peak Scr ($r = -0.59$; 95% CI −0.82 to −0.19; $p = 0.008$) and the estimated GFR (the Schwartz method) at the age of 2 years. (b) There is a significant correlation between the nadir Scr during the first year of life ($r = -0.67$; 95% CI −0.85 to −0.34; $p = 0.0007$) and the estimated GFR (the Schwartz method) at 2 years of life.

Table 3. Nephro-urological outcome in neonates, diagnosed with posterior urethral valves.

	All patients (39)	Prenatal diagnosis (29/39)	Postnatal diagnosis (10/39)
Age at last FU (years)	5.5 (0.02–23)	5 (0.02–17)	11 (2–23)
Measured GFR 2 years (ml/min/1.73 m^2) ($n = 22$)	73 (27.0–182.0)	78.5 (56–150)	61 (27–103)
Estimated GFR 2 years (ml/min/1.73 m^2) ($n = 27$)	76.9 (10.5–203.1)	77.3 (10.5–149.9)	66.2 (16.1–203.1)
Estimated GFR last FU (ml/min/1.73 m^2) ($n = 32$)	81.9 (31.0–118.0)	82.5 (10.5–204)	71.7 (5–106)
CKD ≥ 3 at 2 years	3/26 (11%)	1/19 (5%)	2/7 (28%)
CKD ≥ 3 at latest FU	7/36 (19%)	4/26 (15%)	3/10 (30%)
Dialysis	3/36 (8.3%)	1/26 (4%)	2/10 (20%)
Kidney transplantation	4/36 (11%)	1/26 (4%)	3/10 (30%)
Timing bladder catheterization (day)	1 (0–120)	0 (0–21)	21 (0–120)
Timing endoscopic ablation (day)	45 (6–480)	30 (6–480)	120 (45–330)
Redo ablation	9/36 (25%)	5/26 (19%)	4/10 (40%)
Ureter reimplantation	17/37 (46%)	12/26 (46%)	5/11 (45%)
Other urological interventions	13/36 (36%)		
Number of urological interventions	1 (0–4)	1 (0–4)	1 (0–4)
Persistent diurnal incontinence ≥5 years of age	11/33 (33%)	6/22 (27%)	5/11 (45%)
Intermittent catheterizations	9/32 (28%)	7/25 (28%)	2/7 (28%)
Arterial hypertension	9/36 (25%)	6/25 (24%)	3/11 (27%)

Figure 1. Patient flow chart.

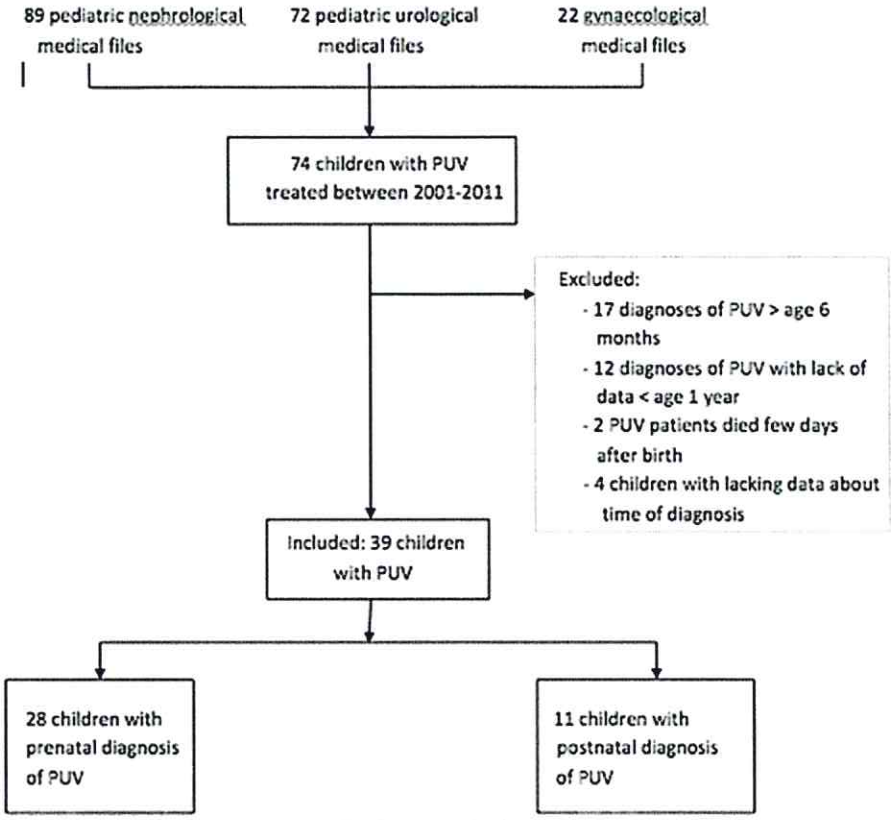

Table 1. Perinatal characteristics in neonates, diagnosed with PUV.

	All cases (39)	Prenatal diagnosis (29/39)	Postnatal diagnosis (10/39)
Prenatal			
Oligohydramnios	13/32 (40%)	13/25 (52%)	0/7 (0%)
Betamethasone	6/24 (25%)	6/23 (26%)	0/1 (0%)
Pre-eclampsia	1/31 (3.2%)	1/25 (4%)	0/6 (0%)
At birth			
GA (weeks)	36 (29–40)	35.45 (29–40)	37 (36–38)
Birth weight (g)	2900 (1310–3950)	2860 (1310–3950)	3010 (2700–3220)
Length (cm)	47 (38.5–54)	47 (38.5–54)	
Apgar 1 min	8 (3–9)	8 (3–9)	
Apgar 5 min	9 (7–10)	9 (7–10)	
Postnatal			
Lung hypoplasia	8/27 (30%)	8/22 (36%)	0/5 (0%)
Oxygen need (days)	0 (0–6)	0 (0–6)	0 (0–0)
Ventilation (days)	0 (0–13)	0 (0–13)	0 (0–0)
Surfactant	2/19 (14%)	2/18 (11%)	0/1 (0%)
Cardiac comorbidity	7/24 (29%)	6/20 (30%)	1/4 (25%)
Neurological comorbidity	2/22 (9.1%)	2/19 (11%)	0/3 (0%)
Gastroenteral comorbidity	5/18 (28%)	5/17 (29%)	0/1 (0%)
Peritoneal dialysis	1/26 (4%)	0/22 (0%)	1/4 (25%)
Urosepsis	13/36 (36%)	5/26 (19%)	8/10 (80%)
Other infections	1/23 (4%)	1/20 (5%)	0/3 (0%)

Risk factors for unfavorable renal outcome

Prenatal diagnosis was neither a risk nor a protecting factor for subsequent unfavorable renal outcome. In contrast, Scr values in early infancy, including all neonatal Scr values from day 9 till day 42, peak Scr (median 1.60 mg/dl, range 0.67–6.50 mg/dl; Figure 2a) and nadir Scr (median 0.49 mg/dl, range 0.17–2.21 mg/dl; Figure 2b) correlated (all at least $p < 0.05$) with the estimated GFR (Schwartz formula) (median 76.6 ml/min/1.73 m^2; range 10.5–203.1 ml/min/1.73 m^2; Table 3) at the age of 2 years. Similar, peak Scr ($r = -0.62$) and Scr at 2 weeks of age ($r = -0.58$) ($p = 0.018$ and 0.037, respectively) correlated with the measured GFR (CrEDTA or inulin clearance) (median 73.5 ml/min/1.73 m^2; range 27–182 ml/min/1.73 m^2; Table 3) at 2 years.

We deducted from our results that a nadir Scr >1 mg/dl was predictive of an unfavorable renal outcome. In the current cohort, nadir Scr was attained around median age 5 months (range 1.5–12 months). However, to have an earlier estimate than nadir Scr, we found that the median decrease from the

University Hospitals Leuven during a 10-year period (2001–2011), an electronic search was performed in the clinical database of the University Hospitals Leuven with this search item. The study population was subsequently divided in two groups, depending on whether or not a prenatal diagnosis was made. Clinical characteristics were extracted from maternal, neonatal, and pediatric file review.

Maternal charts were searched for oligohydramnios, interventions during pregnancy, the presence of pre-eclampsia, and prenatal betamethasone administration. Neonatal charts were reviewed for characteristics at birth (GA, birth weight, and Apgar score) and for morbidities during neonatal stay [duration of ventilation (in days), additional oxygen need (in days), urinary tract infections or (uro)sepsis during the neonatal period and associated co-morbidities]. Pediatric charts were reviewed for timing of bladder decompression and urethral valve ablation, for characteristics of nephro-urological morbidities. This latter included arterial hypertension (defined as blood pressure above the 95th centile reference values correlated with height and age [13]), urinary incontinence (defined as persistent diurnal incontinence >5 years of age), VUR (grades of VUR defined by imaging on voiding cystoureterography (VCUG) (International Reflux Study in Children) [14]. Medical files were also searched for the need for other interventions (urological interventions, medication, and dialysis or renal transplantation).

Charts were also searched for neonatal Scr measurements and indicators of renal function throughout pediatric life. Neonatal Scr values in the first 9 d (including peak Scr) and further on week 2, week 3, week 4, and week 6 of life were collected, similar to the approach applied in neonatal reference populations and in a cohort of extreme low birth weight infants [8,15]. Scr values of the PUV cohort were compared with Scr values of this reference population of similar age and weight. Indicators of renal function after early infancy were Scr values, including the nadir Scr (lowest Scr value in the first year of life), and glomerular filtration rate (GFR) values (either using CrEDTA or inuline clearance), while the Schwartz method [16] was applied to estimate GFR on a yearly basis. In line with the National Kidney Foundation Kidney Disease Outcomes Quality Initiative Classification [17], the estimated and/or measured GFR at the age of 2 years was classified as 'unfavorable renal outcome' if the GFR was below 60 ml/min/1.73 m^2, equal to CKD stage 3 or more. We evaluated the stage of CKD at the age of 2 years and/or at the last follow-up, since at the age of 2 years, GFR is comparable with the GFR in adult life.

Statistical analysis

Scr values, GFR, and population characteristics were described by median and range, resulting in a Scr percentile curve with values for our PUV patients. Uni-variate analysis (Chi-square and Mann–Whitney *U* test) was used to compare prenatal with postnatal diagnosis and to search for significant covariates of peak Scr correlations (Spearman) between Scr values in early infancy and estimated or measured GFR at the age of 2 years were explored [17].

To further test the probability that a given neonatal Scr value predicts unfavorable renal outcome at 2 years, Scr values in neonates of the PUV cohort were compared with available Scr values in a reference population of neonates, admitted in our neonatal intensive and medium care unit [15]. Considering both body weight and postnatal age, we classified individual peak Scr in PUV cases as either above or below the 75th and 90th centile of this reference population [1,8,28]. The same analysis was repeated based on the peak Scr in all individual PUV cases, either above or below the 75th centile of the current PUV cohort. Analysis was performed using MedCalc® program (Mariakerke, Gent, Belgium), a p-value <0.05 was considered to be significant.

Results

Figure 1 provides a flow diagram on the number of cases considered and evaluated. Based on 74 children, 39 patients with PUV were included, of whom 28 had a prenatal diagnosis, and 11 had a postnatal diagnosis.

Perinatal characteristics and postnatal Scr trends

Perinatal data were available in 32/39 patients (25/28 prenatal; 7/11 postnatal diagnosis). Clinical characteristics are provided in Table 1. All prenatal diagnosed cases – except one – presented with bilateral hydronephrosis. Thirteen (40%) pregnancies were complicated by oligohydramnios, including two with anhydramnios. Seven patients (20%) underwent at least one fetal intervention: vesico-amniotic shunt ($n=5$), fetal bladder drainage ($n=1$), and amnion-infusions ($n=2$). In postnatal cases, the diagnosis of PUV was made following (uro)sepsis, presenting at a median age of 4 weeks (range 6 d–4 months). The number of Scr observations, percentiles, and range for consecutive Scr measurements in neonates (prenatal and postnatal diagnosis) are provided in Table 2. Peak Scr (1.6, range 0.67–6.5 mg/dl) occurred on days 3–4. In postnatal cases, this was 2.53 (range 1.59–6.5 mg/dl) on day 15 (range 5–28). The nadir Scr of all patients (0.49, range 0.17–2.21 mg/dl) was observed at a median age of 5 (range 1.5–12) months.

Nephro-urological outcome

The nephro-urological outcome of this PUV cohort is described in Table 3. An unfavorable renal prognosis [GFR <60 ml/min/1.73 m^2 or ≥CKD Stage 3] was documented in 3/26 (11%) infants at 2 years of age and in 7 (19%) children at latest follow up. At 2 years, 6/26 toddlers were classified with CKD Stage 1 (23%), 17 with Stage 2 (65%), 0 with Stage 3 (0%), 2 with Stage 4 (7%), and 1 CKD stage 5 (4%, dialysis at 1.5 years, transplanted at 2.8 years) (median GFR at 2 years = 76.6 ml/min/1.73 m^2; CI 68.9–87.8 ml/min/1.73 m^2). At latest follow-up (median age 5.75 years, 0.02–23 year), of our 36 children, 11 had CKD Stage 1 (30.5%), 17 Stage 2 (47%), 4 CKD Stage 3 (11%), and 3 were classified with CKD Stage 5 or end stage renal disease (ESRD) (8%) (median GFR = 78 ml/min/1.73 m^2; 95% CI = 68–90 ml/min/1.73 m^2). Urinary incontinence was documented in 11 children (33%), nine of them underwent intermittent catheterization. Almost all children had severe VUR, 17 (46%) underwent ureter reimplantation. Arterial hypertension was documented in nine children (25%).

Declaration of interest

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References

1. Sarhan OM, El-Ghoneimi AA, Helmy TE, et al. Posterior urethral valves: multivariate analysis of factors affecting the final renal outcome. J Urol 2011;185:2491–5.
2. Drozdz D, Drozdz M, Gretz N, et al. Progression to end-stage renal disease in children with posterior urethral valves. Pediatr Nephrol 1998;12:630–6.
3. Hennus PM, van der Heijden GJ, Bosch JL, et al. A systematic review on renal and bladder dysfunction after endoscopic treatment of infravesical obstruction in boys. PLoS One 2012;7:e44663.
4. Denes ED, Barthold JS, Gonzalee R. Early prognostic value of serum creatinine levels in children with posterior urethral valves. J Urol 1997;157:1441–3.
5. Deshpande AV, Alsaywid BS, Smith GH. Setting the speed limit: a pilot study of the rate of serum creatinine decrease after endoscopic valve ablation in neonates. J Urol 2011;185:2497–501.
6. Lopez Pereira P, Espinosa L, Martinez Urrutina MJ, et al. Posterior urethral valves: prognostic factors. BJU Int 2003;91:687–90.
7. Nickavar A, Otoukesh H, Sotoudeh K. Validation of initial serum creatinine as a predictive factor for development of end stage renal disease in posterior urethral valves. Indian J Pediatr 2008;75:695–7.
8. Pohl M, Mentzel HJ, Vogt S, et al. Risk factors for renal insufficiency in children with urethral valves. Pediatr Nephrol 2012;27:443–50.
9. Sarhan O, El-Dahsanhan K, Sarhan M. Prognostic value of serum creatinine levels in children with posterior urethral valves treated by primary valve ablation. J Pediatr Urol 2010;6:11–14.
10. Allegaert K, Kuppens M, Mekahli D, et al. Creatinine reference values in ELBW infants: impact of quantification by Jaffe or enzymatic method. J Matern Fetal Neonatal Med 2012;25:1678–81.
11. Cuzzolin L, Fanos V, Pinna B, et al. Postnatal renal function in preterm newborns: a role of diseases, drugs and therapeutic interventions. Pediatr Nephrol 2006;21:931–8.
12. Boer DP, de Rijke YB, Hop WC, et al. Reference values for serum creatinine in children younger than 1 year of age. Pediatr Nephrol 2010;25:2107–13.
13. Gajewski K. Cardiology. In: Tschudy M, Arcara K, eds. The Harriet lane handbook. 19th ed. Philadelphia: Elsevier Mosby; 2012: 160–3.
14. Lebowitz RL, Olbing H, Parkkulaien KV, et al. International system of radiographic grading of vesicoureteric reflux. International Reflux Study in Children. Pediatr Radiol 1985;15:105–9.
15. Allegaert K, Keltemans J, Hendrickx S, Smits A. (2001). Available from: http://trabajos.cin2011.uninet.edu/162/allegaert.pdf.
16. Levey AS, Stevens LA, Schmid CH, et al. A new equation to estimate GFR. In: Stockman J, ed. Yearbook of pediatrics. Philadelphia: Elsevier Mosby; 2011:193–4.
17. Hogg RJ, Furth S, Lemley KV, et al; National Kidney Foundation's Kidney Disease Outcomes Quality Initiative. National Kidney Foundation's Kidney Disease Outcomes Quality Initiative clinical practice guidelines for chronic kidney disease in children and adolescents: evaluation, classification, and stratification. Pediatrics 2003;111:1416–21.
18. Ansari MS, Gulia A, Srivastava A, Kapoor R. Risk factors for progression to end stage renal disease in children with posterior urethral valves. J Pediatr Urol 2010;6:261–4.
19. Ducan L, Heathcote J, Djurdjev O, Levin A. Screening for renal disease using serum creatinine: who are we missing? Nephrol Dial Transplant 2001;16:1042–6.
20. Mandelia A, Bajpai M, Agarwala S, et al. The role of urinary TGF-β1, TNF-α, IL-6 and microalbuminuria for monitoring therapy in posterior urethral valves. Pediatr Nephrol 2013;28:1991–2001.
21. Klein J, Lacroix C, Caubet C, et al. Fetal urinary peptides to predict postnatal outcome of renal disease in fetuses with Posterior Urethral Valves (PUV). Sci Transl Med 2013;6:198–106.
22. Morris RK, Malin GL, Quinlan-Jones E, et al. For the percutaneous vesicoamniotic shunting in Lower Urinary Tract Obstruction (PLUTO) Collaborative Group. Percutaneous vesicoamniotic shunting versus conservative management for fetal lower urinary tract obstruction (PLUTO): a randomised trial. Lancet 2013. pii: S0140-6736(13)60992-7. [Epub ahead of print]. doi:10.1016/S0140-6736(13)60992-7.